WO 2005/014822 PCT/EP2004/051715 1/64

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55	Ser	Tyr	Pro	Asp	Glu	Lys	Asn	Lys	Arg	Ala	Ser	Val	Arg	Arg	Arg	Ile

245 250 255 Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile 5 Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg 280 285 10 Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His 15 <210> 11 <211> 1042 <212> PRT <213> Artificial sequence 20 <220> <223> <400> 11 Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Trp Val Pro 25 Gly Ser Thr Gly Asp Gly Pro Pro Val Ser Cys Ile Lys Arg Asp Ser 30 20 25 Pro Ile Gln Cys Ile Gln Ala Ile Ala Glu Asn Arg Ala Asp Ala Val 35 40 35 Thr Leu Asp Gly Gly Phe Ile Tyr Glu Ala Gly Leu Ala Pro Tyr Lys 50 55 40 Leu Arg Pro Val Ala Ala Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg 70 45 Thr His Tyr Tyr Ala Val Ala Val Val Lys Lys Gly Gly Ser Phe Gln Leu Asn Glu Leu Gln Gly Leu Lys Ser Cys His Thr Gly Leu Arg Arg 50 100 105 Thr Ala Gly Trp Asn Val Pro Ile Gly Thr Leu Arg Pro Phe Leu Asn 115 120 55

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	Trp	Thr 130	Gly	Pro	Pro	Glu	Pro 135	Ile	Glu	Ala	Ala	Val 140	Ala	Arg	Phe	Phe
5	Ser 145	Ala	Ser	Cys	Val	Pro 150	Gly	Ala	Asp	Lys	Gly 155	Gln	Phe	Pro	Asn	Leu 160
10	Суз	Arg	Leu	Cys	Ala 165	Gly	Thr	Gly	Glu	Asn 170	Lys	Cys	Ala	Phe	Ser 175	Ser
15	Gln	Glu	Pro	Tyr 180	Phe	Ser	Tyr	Ser	Gly 185	Ala	Phe	Lys	Cys	Leu 190	Arg	Asp
20	Gly	Ala	Gly 195	Asp	Val	Ala	Phe	Ile 200	Arg	Glu	Ser	Thr	Val 205	Phe	Glu	Asp
25	Leu	Ser 210	Asp	Glu	Ala	Glu	Arg 215	Asp	Glu	Tyr	Glu	Leu 220	Leu	Cys	Pro	Asp
25	Asn 225	Thr	Arg	Lys	Pro	Val 230	Asp	Lys	Phe	Lys	Asp 235	Cys	His	Leu	Ala	Arg 240
30	Val	Pro	Ser	His	Ala 245	Val	Val	Ala	Arg	Ser 250	Val	Asn	Gly	Lys	Glu 255	Asp
35	Ala	Ile	Trp	Asn 260	Leu	Leu	Arg	Gln	Ala 265	Gln	Glu	Lys	Phe	Gly 270	Lys	Asp
40	Lys	Ser	Pro 275	Lys	Phe	Gln	Leu	Phe 280	Gly	Ser	Pro	Ser	Gly 285	Gln	Lys	Asp
	Leu	Leu 290	Phe	Lys	Asp	Ser	Ala 295	Ile	Gly	Phe	Ser	Arg 300	Val	Pro	Pro	Arg
45	Ile 305	Asp	Ser	Gly	Leu	Tyr 310	Leu	Gly	Ser	Gly	Tyr 315	Phe	Thr	Ala	Ile	Gln 320
50	Asn	Leu	Arg	Lys	Ser 325	Glu	Glu	Glu	Val	Ala 330	Ala	Arg	Arg	Ala	Arg 335	Val
55	Val	Trp	Cys	Ala 340	Val	Gly	Glu	Gln	Glu 345	Leu	Arg	Lys	Cys	Asn 350	Gln	Trp

5	Ser	Gly	Leu 355	Ser	Glu	Gly	Ser	Val 360	Thr	Cys	Ser	Ser	Ala 365	Ser	Thr	Thr
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10	Leu 385	Asp	Gly	Gly	Tyr	Val 390	Tyr	Thr	Ala	Gly	Lys 395	Суѕ	Gly	Leu	Val	Pro 400
15	Val	Leu	Ala	Glu	Asn 405	Tyr	Lys	Ser	Gln	Gln 410	Ser	Ser	Asp	Pro	Asp 415	Pro
20	Asn	Cys	Val	Asp 420	Arg	Pro	Val	Glu	Gly 425	Tyr	Leu	Ala	Val	Ala 430	Val	Val
25	Arg	Arg	Ser 435	Asp	Thr	Ser	Leu	Thr 440	Trp	Asn	Ser	Val	Lys 445	Gly	Lys	Lys
	Ser	Cys 450	His	Thr	Ala	Val	Asp 455	Arg	Thr	Ala	Gly	Trp 460	Asn	Ile	Pro	Met
30	Gly 465	Leu	Leu	Phe	Asn	Gln 470	Thr	Gly	Ser	Cys	Lys 475	Phe	Asp	Glu	Tyr	Phe 480
35	Ser	Gln	Ser	Cys	Ala 485	Pro	Gly	Ser	Asp	Pro 490	Arg	Ser	Asn	Leu	Cys 495	Ala
40	Leu	Cys	Ile	Gly 500	Asp	Glu	Gln	Gly	Glu 505	Asn	Lys	Cys	Val	Pro 510	Asn	Ser
45	Asn	Glu	Arg 515	Tyr	Tyr	Gly	Tyr	Thr 520	Gly	Ala	Phe	Arg	Cys 525	Leu	Ala	Glu
	Asn	Ala 530	Gly	Asp	Val	Ala	Phe 535	Val	Lys	Asp	Val	Thr 540	Val	Leu	Gln	Asn ,
50	Thr 545	Asp	Gly	Asn	Asn	Asn 550	Glu	Ala	Trp	Ala	Lys 555	Asp	Leu	Lys	Leu	Ala 560
55	Asp	Phe	Ala	Leu	Leu	Cys	Leu	Asp	Gly	Lys	Arg	Lys	Pro	Val	Thr	Glu

Ala Arg Ser Cys His Leu Ala Met Ala Pro Asn His Ala Val Val Ser Arg Met Asp Lys Val Glu Arg Leu Lys Gln Val Leu Leu His Gln Gln Ala Lys Phe Gly Arg Asn Gly Ser Asp Cys Pro Asp Lys Phe Cys Leu Phe Gln Ser Glu Thr Lys Asn Leu Leu Phe Asn Asp Asn Thr Glu Cys Leu Ala Arg Leu His Gly Lys Thr Thr Tyr Glu Lys Tyr Leu Gly Pro Gln Tyr Val Ala Gly Ile Thr Asn Leu Lys Lys Cys Ser Thr Ser Pro Leu Leu Glu Ala Cys Glu Phe Leu Arg Lys Val Pro Pro Leu Val Lys Val Thr His His Val Thr Ser Ser Val Thr Thr Leu Arg Cys Arg Ala Leu Asn Tyr Tyr Pro Gln Asn Ile Thr Met Lys Trp Leu Lys Asp Lys Gln Pro Met Asp Ala Lys Glu Phe Glu Pro Lys Asp Val Leu Pro Asn Gly Asp Gly Thr Tyr Ser Lys Leu Lys Asp Pro Glu Leu Ser Leu Lys 740. Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro Glu Met Val Ser Lys

Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser 985 990 Val Arg Arg Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr 1000 1005

Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys Asp Lys Gly Leu 1015 5 Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn 1030 10 Thr Ser Val His 1040 <210> 12 15 <211> 597 <212> PRT <213> Artificial sequence <220> <223> 20 <400> 12 Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Trp Val Pro 25 Gly Ser Thr Gly Asp Arg Leu Leu Arg Ser His Ser Leu His Tyr Leu 25 20 30 Phe Met Gly Ala Ser Glu Gln Asp Leu Gly Leu Ser Leu Phe Glu Ala 35 40 35 Leu Gly Tyr Val Asp Asp Gln Leu Phe Val Phe Tyr Asp His Glu Ser 60 50 55 Arg Arg Val Glu Pro Arg Thr Pro Trp Val Ser Ser Arg Ile Ser Ser 40 70 Gln Met Trp Leu Gln Leu Ser Gln Ser Leu Lys Gly Trp Asp His Met 45 Phe Thr Val Asp Phe Trp Thr Ile Met Glu Asn His Asn His Ser Lys 100 105 50 Glu Ser His Thr Leu Gln Val Ile Leu Gly Cys Glu Met Gln Glu Asp 120 115

Asn Ser Thr Glu Gly Tyr Trp Lys Tyr Gly Tyr Asp Gly Gln Asp His

		130					135					140				
5	Leu 145	Glu	Phe	Cys	Pro	Asp 150	Thr	Leu	Asp	Trp	Arg 155	Ala	Ala	Glu	Pro	Arg 160
10	Ala	Trp	Pro	Thr	Lуs 165	Leu	Glu	Trp	Glu	Arg 170	His	Lys	Ile	Arg	Ala 175	Arg
	Gln	Asn	Arg	Ala 180	Tyr	Leu	Glu	Arg	Asp 185	Суз	Pro	Ala	Gln	Leu 190	Gln	Gln
15	Leu	Leu	Glu 195	Leu	Gly	Arg	Gly	Val 200	Leu	Asp	Gln	Gln	Val 205	Pro	Pro	Leu
20	Val	Lys 210	Val	Thr	His	His	Val 215	Thr	Ser	Ser	Val	Thr 220	Thr	Leu	Arg	Cys
25	Arg 225	Ala	Leu	Asn	Tyr	Tyr 230	Pro	Gln	Asn	Ile	Thr 235	Met	Lys	Trp	Leu	Lys 240
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	Pro	Asn	Gly	Asp 260	Gly	Thr	Tyr	Gln	Gly 265	Trp	Ile	Thr	Leu	Ala 270	Val	Pro
35	Pro	Gly	Glu 275	Glu	Gln	Arg	Tyr	Thr 280	Cys	Gln	Val	Glu	His 285	Pro	Gly	Leu
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45	Ser 305	Leu	Lys	Gly	Thr	Gln 310	His	Ile	Met	Gln	Ala 315	Gly	Gln	Thr	Leu	His 320
50	Leu	Gln	Cys	Arg	Gly 325	Glu	Ala	Ala	His	Lys 330	Trp	Ser	Leu	Pro	Glu 335	Met
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	Arg	Asn	Gly 355	Lys	Gln	Phe	Cys	Ser 360	Thr	Leu	Thr	Leu	Asn 365	Thr	Ala	Gln
5	Ala	Asn 370	His	Thr	Gly	Phe	Tyr 3 75	Ser	Cys	Lys	Tyr	Leu 380	Ala	Val	Pro	Thr
10	Ser 385	Lys	Lys	Lys	Glu	Thr 390	Glu	Ser	Ala	Ile	Tyr 395	Ile	Phe	Ile	Ser	Asp 400
15	Thr	Gly	Arg	Pro	Phe 405	Val	Glu	Met	Tyr	Ser 410	Glu	Ile	Pro	Glu	Ile 415	Ile
	His	Met	Thr	Glu 420	Gly	Arg	Glu	Leu	Val 425	Ile	Pro	Cys	Arg	Val 430	Thr	Ser
20	Pro	Asn	Ile 435	Thr	Val	Thr	Leu	Lys 440	Lys	Phe	Pro	Leu	Asp 445	Thr	Leu	Ile
25	Pro	Asp 450	Gly	Lys	Arg	Ile	Ile 455	Trp	Asp	Ser	Arg	Lys 460	Gly	Phe	Ile	Ile
30	Ser 465	Asn	Ala	Thr	Tyr	Lys 470	Glu	Ile	Gly	Leu	Leu 475	Thr	Cys	Glu	Ala	Thr 480
35	Val	Asn	Gly	His	Leu 485	Tyr	Lys	Thr	Asn	Tyr 490	Leu	Thr	His	Arg	Gln 495	Thr
	Asn	Thr	Ile	Ile 500	Asp	Val	Gln	Ile	Ser 505	Thr	Pro	Arg	Pro	Val 510	Lys	Leu
40	Leu	Arg	Gly 515	His	Thr	Leu	Val	Leu 520	Asn	Cys	Thr	Ala	Thr 525	Thr	Pro	Leu
45	Asn	Thr 530	Arg	Val	Gln	Met	Thr 535	Trp	Ser	Tyr	Pro	Asp 540	Glu	Lys	Asn	Lys
50	Arg 545	Ala	Ser	Val	Arg	Arg 550	Arg	Ile	Asp	Gln	Ser 555	Asn	Ser	His	Ala	Asn 560
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Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val 5 Asn Thr Ser Val His 595 10 <210> 13 <211> 1042 <212> PRT <213> Artificial sequence <220> 15 <223> <400> 13 Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro 20 Gly Ser Thr Gly Asp Ser Lys Leu Lys Asp Pro Glu Leu Ser Leu Lys 25 Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr Leu His Leu Gln Cys 30 Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro Glu Met Val Ser Lys 50 35 Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr Ala Gln Ala Asn His 40 85 Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val Pro Thr Ser Lys Lys 100 105 110 45 Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile Ser Asp Thr Gly Arg 115 120 50 Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr 130

Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile

	145					150					155					160
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10	Lys	Arg	Ile	Ile 180	Trp	Asp	Ser	Arg	Lys 185	Gly	Phe	Ile	Ile	Ser 190	Asn	Ala
	Thr	Tyr	Lys 195	Glu	Ile	Gly	Leu	Leu 200	Thr	Cys	Glu	Ala	Thr 205	Val	Asn	Gly
15	His	Leu 210	Tyr	Lys	Thr	Asn	Tyr 215	Leu	Thr	His	Arg	Gln 220	Thr	Asn	Thr	Ile
20	Ile 225	Asp	Val	Gln	Ile	Ser 230	Thr	Pro	Arg	Pro	Val 235	Lys	Leu	Leu	Arg	Gly 240
25	His	Thr	Leu	Val	Leu 245	Asn	Cys	Thr	Ala	Thr 250	Thr	Pro	Leu	Asn	Thr 255	Arg
30	Val	Gln	Met	Thr 260	Trp	Ser	Tyr	Pro	Asp 265	Glu	Ьуs	Asn	Lys	Arg 270	Ala	Ser
	Val	Arg	Arg 275	Arg	Ile	Asp	Gln	Ser 280	Asn	Ser	His	Ala	Asn 285	Ile	Phe	Tyr
35	Ser	Val 290	Leu	Thr	Ile	Asp	Lys 295	Met	Gln	Asn	Lys	Asp 300	Lys	Gly	Leu	Tyr
40	Thr 305	Cys	Arg	Val	Arg	Ser 310	Gly	Pro	Ser	Phe	Lys 315	Ser	Val	Asn	Thr	Ser 320
45	Val	His	Gly	Pro	Pro 325	Val	Ser	Cys	Ile	Lys 330	Arg	Asp	Ser	Pro	Ile 335	Gln
50	Cys	Ile	Gln	Ala 340	Ile	Ala	Glu	Asn	Arg 345	Ala	Asp	Ala	Val	Thr 350	Leu	Asp
	Gly	Gly	Phe 355	Ile	Tyr	Glu	Ala	Gly 360	Leu	Ala	Pro	Tyr	Lys 365	Leu	Arg	Pro

Val Ala Ala Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg Thr His Tyr Tyr Ala Val Ala Val Lys Lys Gly Gly Ser Phe Gln Leu Asn Glu Leu Gln Gly Leu Lys Ser Cys His Thr Gly Leu Arg Arg Thr Ala Gly 10 410 Trp Asn Val Pro Ile Gly Thr Leu Arg Pro Phe Leu Asn Trp Thr Gly 425 15 Pro Pro Glu Pro Ile Glu Ala Ala Val Ala Arg Phe Phe Ser Ala Ser 440 20 Cys Val Pro Gly Ala Asp Lys Gly Gln Phe Pro Asn Leu Cys Arg Leu 25 Cys Ala Gly Thr Gly Glu Asn Lys Cys Ala Phe Ser Ser Gln Glu Pro Tyr Phe Ser Tyr Ser Gly Ala Phe Lys Cys Leu Arg Asp Gly Ala Gly 30 490 Asp Val Ala Phe Ile Arg Glu Ser Thr Val Phe Glu Asp Leu Ser Asp 500 505 35 Glu Ala Glu Arg Asp Glu Tyr Glu Leu Leu Cys Pro Asp Asn Thr Arg 515 520 40 Lys Pro Val Asp Lys Phe Lys Asp Cys His Leu Ala Arg Val Pro Ser 530 535 45 His Ala Val Val Ala Arg Ser Val Asn Gly Lys Glu Asp Ala Ile Trp 545 550 555 560 Asn Leu Leu Arg Gln Ala Gln Glu Lys Phe Gly Lys Asp Lys Ser Pro 50 Lys Phe Gln Leu Phe Gly Ser Pro Ser Gly Gln Lys Asp Leu Leu Phe 55

Lys Asp Ser Ala Ile Gly Phe Ser Arg Val Pro Pro Arg Ile Asp Ser 5 Gly Leu Tyr Leu Gly Ser Gly Tyr Phe Thr Ala Ile Gln Asn Leu Arg 615 10 Lys Ser Glu Glu Glu Val Ala Ala Arg Arg Ala Arg Val Val Trp Cys Ala Val Gly Glu Gln Glu Leu Arg Lys Cys Asn Gln Trp Ser Gly Leu 15 Ser Glu Gly Ser Val Thr Cys Ser Ser Ala Ser Thr Thr Glu Asp Cys 20 Ile Ala Leu Val Leu Lys Gly Glu Ala Asp Ala Met Ser Leu Asp Gly 25 Gly Tyr Val Tyr Thr Ala Gly Lys Cys Gly Leu Val Pro Val Leu Ala 695 30 Glu Asn Tyr Lys Ser Gln Gln Ser Ser Asp Pro Asp Pro Asn Cys Val 710 715 Asp Arg Pro Val Glu Gly Tyr Leu Ala Val Ala Val Val Arg Arg Ser 35 Asp Thr Ser Leu Thr Trp Asn Ser Val Lys Gly Lys Lys Ser Cys His 745 40 Thr Ala Val Asp Arg Thr Ala Gly Trp Asn Ile Pro Met Gly Leu Leu 760 45 Phe Asn Gln Thr Gly Ser Cys Lys Phe Asp Glu Tyr Phe Ser Gln Ser 50 Cys Ala Pro Gly Ser Asp Pro Arg Ser Asn Leu Cys Ala Leu Cys Ile 785 790 795 Gly Asp Glu Gln Gly Glu Asn Lys Cys Val Pro Asn Ser Asn Glu Arg 55 805 810

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5	Tyr	Tyr	Gly	Tyr 820	Thr	Gly	Ala	Phe	Arg 825	Cys	Leu	Ala	Glu	Asn 830	Ala	Gly
	Asp	Val	Ala 835	Phe	Val	Lys	Asp	Val 840	Thr	Val	Leu	Gln	Asn 845	Thr	Asp	Gly
10	Asn	Asn 850	Asn	Glu	Ala	Trp	Ala 855	Lys	Asp	Leu	Lys	Leu 860	Ala	Asp	Phe	Ala
15	Leu 865	Leu	Cys	Leu	Asp	Gly 870	Lys	Arg	Lys	Pro	Val 875	Thr	Glu	Ala	Arg	Ser 880
20	Cys	His	Leu	Ala	Met 885	Ala	Pro	Asn	His	Ala 890	Val	Val	Ser	Arg	Met 895	Asp
25	Lys	Val	Glu	Arg 900	Leu	Lys	Gln	Val	Leu 905	Leu	His	Gln	Gln	Ala 910	Lys	Phe
	Gly	Arg	Asn 915	Gly	Ser	Asp	Cys	Pro 920	Asp	Lys	Phe	Суз	Leu 925	Phe	Gln	Ser
30	Glu	Thr 930	Lys	Asn	Leu	Leu	Phe 935	Asn	Asp	Asn	Thr	Glu 940	Cys	Leu	Ala	Arg
35	Leu 945	His	Gly	Lys	Thr	Thr 950	Tyr	Glu	Lys	Tyr	Leu 955	Gly	Pro	Gln	Tyr	Val 960
40	Ala	Gly	Ile	Thr	Asn 965	Leu	Lys	Lys	Cys	Ser 970	Thr	Ser	Pro	Leu	Leu 975	Glu
45	Ala	Cys	Glu	Phe 980	Leu	Arg	Lys	Val	Pro 985	Pro	Leu	Val	Lys	Val 990	Thr	His
	His	Val	Thr 995	Ser	Ser	Val	Thr	Thr 1000		Arg	r Cys	a Arg	7 Ala 100		eu As	sn Tyr
50	Tyr	Pro 1010		a Asn	ılle	. Thi	Met 101	_	s Tı	p Le	eu Ly		sp I 20	ys (Gln E	°ro
55	Met	Asp	Ala	. Lys	Glu	ı Phe	: Glu	ı Pr	ю Гу	rs As	p Va	ıl Le	eu I	?ro P	Asn G	Sly

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Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Arg Leu Leu Arg Ser His Ser Leu His Tyr Leu Phe Met Gly Ala Ser Glu Gln Asp Leu Gly Leu Ser Leu Phe Glu Ala Leu Gly Tyr Val Asp Asp Gln Leu Phe Val Phe Tyr Asp His Glu Ser Arg Arg Val Glu Pro Arg Thr Pro Trp Val Ser Ser Arg Ile Ser Ser Gln Met Trp

5	Leu 385	Gln	Leu	Ser	Gln	Ser 390	Leu	Lys	Gly	Trp	Asp 395	His	Met	Phe	Thr	Val 400
	Asp	Phe	Trp	Thr	Ile 405	Met	Glu	Asn	His	Asn 410	His	Ser	Lys	Glu	Ser 415	His
10	Thr	Leu	Gln	Val 420	Ile	Leu	Gly	Суз	Glu 425	Met	Gln	Glu	Asp	Asn 430	Ser	Thr
15	Glu	Gly	Tyr 435	Trp	Lys	Tyr	Gly	Tyr 440	Asp	Gly	Gln	Asp	His 445	Leu	Glu	Phe
20	Cys	Pro 450	Asp	Thr	Leu	Asp	Trp 455	Arg	Ala	Ala	Glu	Pro 460	Arg	Ala	Trp	Pro
25	Thr 465	Lys	Leu	Glu	Trp	Glu 470	Arg	His	Lys	Ile	Arg 475	Ala	Arg	Gln	Asn	Arg 480
20	Ala	Tyr	Leu	Glu	Arg 485	Asp	Cys	Pro	Ala	Gln 490	Leu	Gln	Gln	Leu	Leu 495	Glu
30	Leu	Gly	Arg	Gly 500	Val	Leu	Asp	Gln	Gln 505	Val	Pro	Pro	Leu	Val 510	Lys	Val
35	Thr	His	His 515	Val	Thr	Ser	Ser	Val 520	Thr	Thr	Leu	Arg	Cys 525	Arg	Ala	Leu
40	Asn	Tyr 530	Tyr	Pro	Gln	Asn	Ile 535	Thr	Met	Lys	Trp	Leu 540	Lys	Asp	Lys	Gln
45	Pro 545	Met	Asp	Ala	Lys	Glu 550	Phe	Glu	Pro	Lys	Asp 555	Val	Leu	Pro	Asn	Gly 560
	Asp	Gly	Thr	Tyr	Gln 565	Gly	Trp	Ile	Thr	Leu 570	Ala	Val	Pro	Pro	Gly 575	Glu
50	Glu	Gln	Arg	Tyr 580	Thr	Cys	Gln	Val	Glu 585	His	Pro	Gly	Leu	Asp 590	Gln	Pro
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595

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20	Pro	Gly	Pro 35	Gly	Gln	Asp	Thr	Asp 40	Суѕ	Arg	Glu	Суѕ	Glu 45	Ser	Gly	Ser
25	Phe	Thr	Ala	Ser	Glu	Asn	His 55	Leu	Arg	His	Cys	Leu 60	Ser	Cys	Ser	Lys
	Cys 65	Arg	Lys	Glu	Met	Gly 70	Gln	Val	Glu	Ile	Ser 75	Ser	Cys	Thr	Val	Asp 80
30	Arg	Asp	Thr	Val	Cys 85	Gly	Суѕ	Arg	Lys	Asn 90	Gln	Tyr	Arg	His	Tyr 95	Trp
35	Ser	Glu	Asn	Leu 100	Phe	Gln	Cys	Phe	Asn 105	Cys	Ser	Leu	Cys	Leu 110	Asn	Gly
40	Thr	Val	His 115	Leu	Ser	Суз	Gln	Glu 120	Lys	Gln	Asn	Thr	Val 125	Cys	Thr	Cys
45	His	Ala 130	Gly	Phe	Phe	Leu	Arg 135	Glu	Asn	Glu	Суз	Val 140	Ser	Cys	Ser	Asn
	Cys 145	Lys	Lys	Ser	Leu	Ġlu 150	Cys	Thr	Lys	Leu	Cys 155	Leu	Pro	Gln	Ile	Glu 160
50	Asn	Val	Lys	Gly	Thr 165	Glu	Asp	Ser	Gly	Thr 170	Thr	Val	Leu	Leu	Pro 175	Leu

 $\,$ Val Ile Phe Phe Gly Leu Cys Leu Leu Ser Leu Leu Phe Ile Gly Leu

180 185 190 Met Tyr Arg Tyr Gln Arg Trp Lys Ser Lys Leu Tyr Ser Ile Val Cys 5 195 200 Gly Lys Ser Thr Pro Glu Lys Glu Gly Glu Leu Glu Gly Thr Thr Thr 10 Lys Pro Leu Ala Pro Asn Pro Ser Phe Ser Pro Thr Pro Gly Phe Thr 15 Pro Thr Leu Gly Phe Ser Pro Val Pro Ser Ser 245 20 <210> 16 <211> 992 <212> PRT <213> Artificial sequence <220> 25 <223> <400> 16 Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Trp Val Pro 30 Gly Ser Thr Gly Asp Gly Pro Pro Val Ser Cys Ile Lys Arg Asp Ser 35 Pro Ile Gln Cys Ile Gln Ala Ile Ala Glu Asn Arg Ala Asp Ala Val 35 40 Thr Leu Asp Gly Gly Phe Ile Tyr Glu Ala Gly Leu Ala Pro Tyr Lys 50 45 Leu Arg Pro Val Ala Ala Glu Val Tyr Gly Thr Glu Arg Gln Pro Arg 65 70 Thr His Tyr Tyr Ala Val Ala Val Lys Lys Gly Gly Ser Phe Gln 50 85 Leu Asn Glu Leu Gln Gly Leu Lys Ser Cys His Thr Gly Leu Arg Arg

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	Pro	Gln	Asn 755	Asn	Ser	Ile	Cys	Cys 760	Thr	Lys	Cys	His	Lys 765	Gly	Thr	Tyr

Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg Glu 775 Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser 10 810 Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln 825 15 Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser 840 20 Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu Lys Gln Asn 855 25 Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys 30 Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser Gly Thr Thr 900 905 35 Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu Leu Ser Leu 920 915 40 Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys Ser Lys Leu 935 930 45 Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu Gly Glu Leu 945 950 955 Glu Gly Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser Phe Ser Pro 50 965 970 Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val Pro Ser Ser 985

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Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp 335 Asp 40 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu 340 Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val 355 Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg 370 Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe 400			Ile	His	Pro	Gln		Asn	Ser	Ile	Cys	_	Thr	Lys	Cys	His	
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Ile Thr Asn Leu Lys Lys Cys Ser Thr Ser Pro Leu Leu Glu Ala Cys 920 5 Glu Phe Leu Arg Lys Val Pro Pro Leu Val Lys Val Thr His His Val 935 10 Thr Ser Ser Val Thr Thr Leu Arg Cys Arg Ala Leu Asn Tyr Tyr Pro 950 15 Gln Asn Ile Thr Met Lys Trp Leu Lys Asp Lys Gln Pro Met Asp Ala 965 970 Lys Glu Phe Glu Pro Lys Asp Val Leu Pro Asn Gly Asp Gly Thr Tyr 20 <210> 19 <211> 547 25 <212> PRT <213> Artificial sequence <220> <223> 30 <400> 19 Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Trp Val Pro 35 Gly Ser Thr Gly Asp Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His 40 Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg Glu 45 Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys 50 Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser 90

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Arg Thr Pro Trp Val Ser Ser Arg Ile Ser Ser Gln Met Trp Leu Gln Leu Ser Gln Ser Leu Lys Gly Trp Asp His Met Phe Thr Val Asp Phe Trp Thr Ile Met Glu Asn His Asn His Ser Lys Glu Ser His Thr Leu Gln Val Ile Leu Gly Cys Glu Met Gln Glu Asp Asn Ser Thr Glu Gly Tyr Trp Lys Tyr Gly Tyr Asp Gly Gln Asp His Leu Glu Phe Cys Pro Asp Thr Leu Asp Trp Arg Ala Ala Glu Pro Arg Ala Trp Pro Thr Lys Leu Glu Trp Glu Arg His Lys Ile Arg Ala Arg Gln Asn Arg Ala Tyr Leu Glu Arg Asp Cys Pro Ala Gln Leu Gln Gln Leu Leu Glu Leu Gly Arg Gly Val Leu Asp Gln Gln Val Pro Pro Leu Val Lys Val Thr His His Val Thr Ser Ser Val Thr Thr Leu Arg Cys Arg Ala Leu Asn Tyr Tyr Pro Gln Asn Ile Thr Met Lys Trp Leu Lys Asp Lys Gln Pro Met Asp Ala Lys Glu Phe Glu Pro Lys Asp Val Leu Pro Asn Gly Asp Gly Thr Tyr Gln Gly Trp Ile Thr Leu Ala Val Pro Pro Gly Glu Gln Arg Tyr Thr Cys Gln Val Glu His Pro Gly Leu Asp Gln Pro Leu Ile

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10	Leu	Ser 210	Asp	Glu	Ala	Glu	Arg 215	Asp	Glu	Tyr	Glu	Leu 220	Leu	Cys	Pro	Asp
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Val Leu Ala Glu Asn Tyr Lys Ser Gln Gln Ser Ser Asp Pro Asp Pro Asn Cys Val Asp Arg Pro Val Glu Gly Tyr Leu Ala Val Ala Val Val 420 425 Arq Arg Ser Asp Thr Ser Leu Thr Trp Asn Ser Val Lys Gly Lys Lys 440 Ser Cys His Thr Ala Val Asp Arg Thr Ala Gly Trp Asn Ile Pro Met Gly Leu Leu Phe Asn Gln Thr Gly Ser Cys Lys Phe Asp Glu Tyr Phe Ser Gln Ser Cys Ala Pro Gly Ser Asp Pro Arg Ser Asn Leu Cys Ala Leu Cys Ile Gly Asp Glu Gln Gly Glu Asn Lys Cys Val Pro Asn Ser 505 Asn Glu Arg Tyr Tyr Gly Tyr Thr Gly Ala Phe Arg Cys Leu Ala Glu 520 Asn Ala Gly Asp Val Ala Phe Val Lys Asp Val Thr Val Leu Gln Asn 535 Thr Asp Gly Asn Asn Asn Glu Ala Trp Ala Lys Asp Leu Lys Leu Ala 550 555

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Asp Phe Ala Leu Leu Cys Leu Asp Gly Lys Arg Lys Pro Val Thr Glu 575

Ala Arg Ser Cys His Leu Ala Met Ala Pro Asn His Ala Val Val Ser 580

Arg Met Asp Lys Val Glu Arg Leu Lys Gln Val Leu Leu His Gln Gln 595

Ala Lys Phe Gly Arg Asn Gly Ser Asp Cys Pro Asp Lys Phe Cys Leu 615

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20	Val	Thr 690	His	His	Val	Thr	Ser 695	Ser	Val	Thr	Thr	Leu 700	Arg	Cys	Arg	Ala
25	Leu 705	Asn	Tyr	Tyr	Pro	Gln 710	Asn	Ile	Thr	Met	Lys 715	Trp	Leu	Lys	Asp	Lys 720
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40	Phe	Pro 770	Ala	Ala	Lys	Gln	Cys 775	Pro	Ala	Leu	Glu	Val 780	Thr	Trp	Pro	Glu
45	Val 785	Glu	Val	Pro		Asn 790	Gly	Thr	Leu	Ser	Leu 795	Ser	Cys	Val	Ala	Cys 800
	Ser	Arg	Phe	Pro	Asn 805	Phe	Ser	Ile	Leu	Tyr 810	Trp	Leu	Gly	Asn	Gly 815	Ser
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845 835 840 Gln Leu Thr Pro Ala Leu His Ser Thr Asn Phe Ser Cys Val Leu Val 5 850 Asp Pro Glu Gln Val Val Gln Arg His Val Val Leu Ala Gln Leu Trp 10 Val Arg Ser Pro Arg Arg Gly Leu Gln Glu Glu Glu Leu Cys Phe 15 His Met Trp Gly Gly Lys Gly Gly Leu Cys Gln Ser Ser Leu 20 <210> 22 <211> 465 <212> PRT <213> Artificial sequence <220> 25 <223> <400> 22 Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro 30 10 15 Gly Ser Thr Gly Asp Arg Leu Leu Arg Ser His Ser Leu His Tyr Leu 25 20 35 Phe Met Gly Ala Ser Glu Gln Asp Leu Gly Leu Ser Leu Phe Glu Ala 35 40 40 Leu Gly Tyr Val Asp Asp Gln Leu Phe Val Phe Tyr Asp His Glu Ser 50 45 Arg Arg Val Glu Pro Arg Thr Pro Trp Val Ser Ser Arg Ile Ser Ser 70 Gln Met Trp Leu Gln Leu Ser Gln Ser Leu Lys Gly Trp Asp His Met 50 Phe Thr Val Asp Phe Trp Thr Ile Met Glu Asn His Asn His Ser Lys 55

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30	Arg 225	Ala	Leu	Asn	Tyr	Tyr 230	Pro	Gln	Asn	Ile	Thr 235	Met	Lys	Trp	Leu	Lys 240
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Ala Ser Val Arg Ser Thr Lys Asp Pro Cys Pro Ser Gln Pro Pro Val 5 Phe Pro Ala Ala Lys Gln Cys Pro Ala Leu Glu Val Thr Trp Pro Glu Val Glu Val Pro Leu Asn Gly Thr Leu Ser Leu Ser Cys Val Ala Cys 10 Ser Arg Phe Pro Asn Phe Ser Ile Leu Tyr Trp Leu Gly Asn Gly Ser 8.5 90 15 Phe Ile Glu His Leu Pro Gly Arg Leu Trp Glu Gly Ser Thr Ser Arg 100 105 20 Glu Arg Gly Ser Thr Gly Thr Gln Leu Cys Lys Ala Leu Val Leu Glu 115 120 25 Gln Leu Thr Pro Ala Leu His Ser Thr Asn Phe Ser Cys Val Leu Val 130 Asp Pro Glu Gln Val Val Gln Arg His Val Val Leu Ala Gln Leu Trp 30 145 Val Arg Ser Pro Arg Arg Gly Leu Gln Glu Glu Glu Leu Cys Phe 165 35 His Met Trp Gly Gly Lys Gly Gly Leu Cys Gln Ser Ser Leu Gly Pro 180 40 Pro Val Ser Cys Ile Lys Arg Asp Ser Pro Ile Gln Cys Ile Gln Ala 195 200 205 45 Ile Ala Glu Asn Arg Ala Asp Ala Val Thr Leu Asp Gly Gly Phe Ile 215 210 Tyr Glu Ala Gly Leu Ala Pro Tyr Lys Leu Arg Pro Val Ala Ala Glu 50 Val Tyr Gly Thr Glu Arg Gln Pro Arg Thr His Tyr Tyr Ala Val Ala 245 250

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15	Ile 305	Glu	Ala	Ala	Val	Ala 310	Arg	Phe	Phe	Ser	Ala 315	Ser	Cys	Val	Pro	Gly 320
20	Ala	Asp	Lys	Gly	Gln 325	Phe	Pro	Asn	Leu	Cys 330	Arg	Leu	Суѕ	Ala	Gly 335	Thr
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15	Val	Thr 530	Cys	Ser	Ser	Ala	Ser 535	Thr	Thr	Glu	Asp	Cys 540	Ile	Ala	Leu	Val
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25	Ser 785	Asp	Cys	Pro	Asp	Lys 790	Phe	Cys	Leu	Phe	Gln 795	Ser	Glu	Thr	Lys	A sn 800	
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	Thr	Thr	Tyr	Glu 820	Lys	Tyr	Leu	Gly	Pro 825	Gln	Tyr	Val	Ala	Gly 830	Ile	Thr	
35	Asn	Leu	Lys 835	Lys	Cys	Ser	Thr	Ser 840	Pro	Leu	Leu	Glu	Ala 845	Cys	Glu	Phe	
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45	Ser 865	Val	Thr	Thr	Leu	Arg 870	Cys	Arg	Ala	Leu	Asn 875	Tyr	Tyr	Pro	Gln	Asn 880	
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Lys Glu Phe Glu Pro Lys Asp Val Leu Pro Asn Gly Asp Gly Thr Tyr 420 425 430

Gln Gly Trp Ile Thr Leu Ala Val Pro Pro Gly Glu Glu Gln Arg Tyr 435 440 445

10

Thr Cys Gln Val Glu His Pro Gly Leu Asp Gln Pro Leu Ile Val Ile 450 455 460

15

Trp 465